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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,397	MOSER ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/13/03, 1/12/04, 3/1/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-24 and 29-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5-24, 29-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's Amendment, Remarks, and 1.132 declaration of Inventor Moser, filed 11/13/03, 1/12/04, and 3/01/04, are acknowledged.

2. The new declaration of Inventor Lespagnard, filed 11/13/03, has been found acceptable.

3. Claims 1, 3, 5-24, and newly added claims 29-50 are pending and are being acted upon.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 3, 19-24, and newly added Claims 29-37, 39-45, and 47-50 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), for the reasons of record as set forth in the action mailed 8/12/03.

Applicant's arguments, filed 11/13/03, have been fully considered but they are not persuasive. Applicant argues, "the feasibility of making the DC/tumor hybrids is not predictable as discussed in the Declaration of Dr. Moser". Accordingly, the declaration will be addressed here.

The declarant argues "In my opinion, based on said documents it is not predictable that such hybrids could be made and which characteristic said hybrids would carry. Furthermore, I am convinced that the approach of Guo for making his hybrids may not be followed to produce hybrids which may be used for human applications. As the method of making said hybrids (and thus also the starting cells) are different it is clear that the resulting hybrids will be different". The declarant continues, "Changing the fusion partner of the tumor cell, as with the B cell of Guo et al. (1994), to another antigen-presenting cell does not allow one of skill in the art to predict the outcome of such an experiment." The declarant cites Carbonne et al. (1988) in support of the arguments. The declarant continues with numerous reasons for the asserted unpredictability.

It is the examiner's position that the Inventor's arguments are not convincing for the following reasons. First, the teachings of Guo et al. must be considered in the context of what one of skill in the art would have known at the time of the invention. Thus, the precise methods of Guo et al. would not need to followed, some variation and routine experimentation would be allowable and still be considered obvious. Additionally, since one of ordinary skill in the art at the time of the invention would have known that DC hybridomas retaining T cell activation capability were produced as early as 1981, (see, for example, the work of J.H. Peters) the declarant cannot convincingly argue that said hybridomas/ hybrids could not be predictably made over a decade later. Regarding the Carbonne et al. reference, a review of said reference shows that the teachings of the reference are not applicable to the instant situation. In that work the authors fused two closely related cells, one which expressed Lyt-2 (CD8) and one which did not. The point of the work was the study of Lyt-2 expression, in particular whether said expression was under positive or negative regulation during T cell development. The authors discovered trans-acting negative regulatory factors specifically provided by the cell that did not express Lyt-2 which shut down expression of the gene in the hybrid. This highly specific situation cannot be generically applied to assert unpredictability in the hybrids employed in the method of the instant claims.

The declarant makes a number of assertions that comprise either unclaimed limitations or irrelevant observations. The declarant describes "major advantages" of the method used in the instant specification to generate the hybrids employed in the method of the instant claims. For example, the declarant presents an argument that Guo et al. employed Freund's complete adjuvant which cannot be administered more than once and which cannot be administered to humans. The declarant further indicates that the method taught by Guo et al. requires the use of an "essential organ" (spleen).

It is the Examiner's position that adjuvants which could be administered more than once and which could be administered to humans were well-known in the art in the middle 1990's, as were sources of DCs besides the spleen. Regardless, note that no claims limiting the claimed method to humans are pending and only a few of the dependent claims limit the source of the DCs to other than spleen. Also, regarding the "major advantages" of the method used in the instant specification to generate the hybrids employed in the method of the instant claims, it is noted that none of the advantages comprise claimed limitations.

Accordingly, said advantages do not render the claimed method non-obvious.

The declarant argues that spleen cells are not a good source of DCs for the production of DC/tumor hybridomas.

This seems a particularly curious argument given the fact that the hybridomas employed in the first six examples of the specification were produced using spleen cells, see page 32, *Example 2: Preparation of Murine Dendritic-Like Cells from the Spleen*. Also, note that this limitation, which the declarant appears to be arguing is critical, is not recited in the independent claims.

The declarant makes an argument regarding the use of GM-CSF to induce DC-characteristics that is unclear to the Examiner. The declarant appears to argue that the use of GM-CSF in the claimed method would not have been obvious.

It is the Examiner's position that the use of GM-CSF in the culture of DC was well-known at the time of the invention and it is unclear to the Examiner why the declarant appears to see some sort of non-obviousness in its use in the method of the instant claims.

The declarant argues "in the present invention it is suggested that said hybrids/hybridomas may be irradiated. However, said irradiation is not an essential step in the production of said vaccine.

It is the Examiner's position that whether or not irradiation is essential, it is still obvious as it is unlikely that any patient would knowingly accept the administration of unattenuated or live tumor hybridomas.

Applicant presents additional arguments. Applicant argues that, "it is only based on the present invention and by using impermissible hindsight that a skilled person may expect that by producing said hybrid/hybridomas, cells may be created having characteristics of both DC and tumor cells which are needed to induce an anti-tumor response in a subject".

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. So long as it takes into account only knowledge which

was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). It remains the Examiner's position that the combined references, in view of that which was known in the art at the time of the invention, render the instant methods obvious and not unpredictable, i.e., the hybrid of Guo et al. was functional, Sornasse et al. taught that DCs were better APCs than B cells, and it was known in the art that DC/tumor hybrids that maintained T cell activating capability could be produced.

Applicant presents an additional argument regarding the source of the DCs.

It is unclear to the Examiner how the source of the DCs could render the method of the instant claims patentably distinct given the fact that blood, bone marrow, and lymph or lymph nodes were all well-known sources of DCs at the time of the invention. Further note, as set forth above, the instant specification employed DCs from spleen in the first 6 examples. Applicant is advised that if it is Applicant's position that splenic DCs be excluded, a limitation to the effect would properly belong in the independent claims.

6. Claims 5-10 and newly added Claims 38 and 46 stand/are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 3, and 19-26 above, and in further view of U.S. Patent No. 5,851,756, for the reasons of record as set forth in the action mailed 8/12/03.

Applicant's arguments, filed 11/13/03, have been fully considered but they are not persuasive. See section 5 above for the Examiner's response.

7. Claims 11-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 3, and 19-26 above, and in further view of U.S. Patent No. 5,637,483, for the reasons of record as set forth in the action mailed 8/12/03.

Applicant's arguments, filed 11/13/03, have been fully considered but they are not persuasive. See section 5 above for the Examiner's response.

8. The following are new grounds for rejection necessitated by Applicant's amendment.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3, 5-24, and newly added claims 29-50 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) a method employing "dendritic cell/tumor hybrids (hybridoma) cell hybrids, wherein said dendritic cell is not a T-lymphocyte, B-lymphocyte, monocyte/macrophage or another non-dendritic cell present in enriched or purified dendritic cell preparations", in Claims 1 and 3.

B) a method wherein the dendritic cell "is purified from lymph or lymph nodes", in Claims 35, 43, 48, and 50.

Applicant's amendment, filed 11/13/03, asserts that support for the new limitations of Claims 1 and 3 can be found at paragraphs 8 and 24 of the published application. No support, however, has been found for the various subgenuses of cells comprising this combination of negative limitations, nor has support been found for the macrophage or "another non-dendritic cell" of the claims. Regarding the dendritic cell "purified from lymph or lymph nodes" of Claims 35, 43, 48, and 50, the specification discloses only a dendritic cell "purified from lymph or accessible lymph nodes".

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 31-46 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically, the phrase "wherein the dendritic cell (or proliferating dendritic cell) is at a more immature stage", is vague and indefinite as it is clear that the metes and bounds of the method comprising this limitation cannot be readily established. It is noted that not even a DC of an "immature stage" is defined in the specification. Increasing the indefiniteness of the claims is that it is not actually an immature DC that is encompassed by the claims, but rather a "more" immature DC.

13. No claim is allowed.

14. Applicant's amendment or action (filing of new applications) necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

16. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

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6/1/04

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